Alem Truneh, Ph.D.
Antigenics Inc., 3 Forbes Road, Lexington, MA 02421
781-674-4420 (Work) 781-820-4030 (Mobile)
atruneh@antigenics.com

CAREER PROFILE

Senior pharmaceutical executive with 20 years of experience in pharmaceutical R&D. Vice President of research and development at Antigenics since 2001. Prior to Antigenics, 17 years of drug discovery and development experience at GlaxoSmithKline (& its heritage companies SB & SKB/SK&F) in several therapeutic areas, including inflammatory, autoimmune and allergic disorders, cancer, and infectious diseases. Helped advance several products, biologics, as well as small molecule drugs (NCEs/NMEs), from early discovery through advanced clinical trials & registration, and post-market product differentiation and PLEs. Served on senior level task forces, strategy teams and scientific and management committees.
Academic background includes Ph.D. in Biological Chemistry, and several years of research experiences in immunology, pharmacology and biochemistry. Academic appointments include Visiting Scientist and EMBO fellow (INSERM/CNRS, France), and associate professor of pharmacy at University of Marseille. Co-authored over 100 scientific papers and co-inventor on 24 issued or pending patents. Organized national and international scientific conferences, is a member of several scientific associations, serves on journal editorial boards and has won many scientific and management awards and honors.

PROFESSIONAL EXPERIENCE

Antigenics ***October 2001 - Present***

Vice President of R&D with responsibility for research and non-clinical development at Antigenics. Current pipeline includes an immunotherapeutic agent (Oncophage) in Phase III clinical development for treatment of cancer (RCC & melanoma), AG-858 an immunotherapeutic for CML, a liposomally formulated platinal (Aroplatin) in Phase II for colorectal cancer, a vaccine in development for treatment of HSV-2 infections, and other candidate products at various stages of non-clinical development.

At Antigenic, re-organized the research and pre-clinical develoment division of scientists and staff, derived from three heritage companies (Antigenics, Acquila & Aronex) on three locations, into a single, integrated and streamlined, matrix based structure, with immediate and positive impact on performance and productivity. As a member of the senior management team, progressed drug candidates through the discovery and development pipeline, helped prioritize projects, with emphasis in oncology and infectious diseases. Established academic collaborations, and obtained NIH SBIR grant funding for ID vaccine development. Managed programs including biologics and small molecule drugs for cancer and infectious diseases. Headed or served on various senior operational or advisory committees.

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GlaxoSmithKline (Heritage Company: SmithKline Beecham Pharmaceuticals) 1984 - 2001

Joined GlaxoSmithKline (formerly SmithKline Beecham & SmithKline Beckman) as junior level scientist and progressed to Director of Immunology with involvement in many areas of drug discovery and development. Highlights of accomplishment during this period at GSK & SB are listed below.

- As Director of Immunology, managed a department of 40 scientists and staff. Helped set scientific directions, developed disease strategies, managed budgets & resources, hired, trained and mentored personnel, and served on senior R&D management and scientific committees.
- Initiated several drug discovery efforts and led large multidisciplinary teams to advance these efforts from target identification through disease association studies, assay development, generation of potential therapeutic agents and in vivo evaluation, progressing them from early discovery through pre-clinical into clinical studies. Progressed 3 compounds into clinical trials and participated on 3 additional NCEs. Helped file over a dozen IND (US) and CTA/CTX (Europe) applications, provided pre-clinical support, including GLP studies, developed clinical surrogate endpoints/biomarkers, and helped with design of clinical trials and data intepretation and participated in regulatory (FDA) meetings. Helped design Market Aligned "development" Plans (MAPs) for drug candidates.
- Participated in product differentiation and PLE efforts.
- Served on publication strategy teams for compounds in clinical development.
- Co-led inter-company discovery efforts.
- Worked with Business Development to review in-licensing and collaborative opportunities (over 200), including participation in strategic reviews of external business opportunities in specific disease catagories, participated in due diligence reviews and led scientific due diligence evaluations.
- Served on process improvement teams, working parties, high level task forces and inter-company steering committees, Strategic Initiatives (GPCRs, Chemokines, Novel TNF/TNFRs, etc), Inflammation Tissue Repair & Oncology - Disease Area Strategic Team (ITRO-DAST; covering autoimmunity, inflammation, osteoarthritis, osteoporosis and oncology with representation from Drug Discovery, Clinical Pharmacology, Clinical Development, Project Management, Business Development and Marketing).
- Established and managed several academic collaborations including sponsored/funded and unfunded projects.
- Helped develop and adopt new technologies in biology, including molecular and cellular, developed *in vivo* models in inflammation, immunology and oncology (e.g. DTH, SCID, MS, psoriasis, IBD, tumor and angiogenesis) and managed core facilities.
- Maintained scientific excellence and visibility through publication of over 70 manuscripts, submission of over 20 patent applications and organizing and/or participation (invited speaker and/or faculty, etc) in scientific meetings, membership of professional societies and associate editorship of scientific journals.

Overall experience gained at GSK/SB includes: drug discovery and development skills with experience in *in vitro* and *in vivo* cellular & molecular biology, increased practical and

theoretical experience in immuno, cell and tumor biology, better understanding of disease processes such as inflammation, autoimmunity, allergic, pulmonary and bone disorders, cancer, HIV/AIDS, experience in small molecule drugs/compounds as well as protein drugs; exposure to strategic, regulatory, business, marketing and legal issues relating to drug discovery and development; leadership of multi-disciplinary teams, and personnel and resource management.

Associate Professor of Pharmacy
Faculté de Pharmacie, Université de la Méditerrané - Aix Marseille II - France 1984

This French Ministry of Education appointment involved both teaching and university funded research with own lab, students and technicians.

EMBO Fellow & Visiting Scientist - INSERM/CNRS - France Jan 1982 – Dec 1983

As an EMBO fellow and Visiting Scientist at the Centre d'Immunologie - INSERM / CNRS in Luminy, France, conducted research in immunology, resulting in 12 scientific publications in prestigious international journals and filing of one patent application. The topics covered in these publications included i) endocytosis and recycling of MHC molecules, ii) activation of and signaling in T cells, iii) adhesion molecules on T and B cells, iv) use of antibody-conjugated drug encapsulating liposomes to kill and/or rescue specific tumor cells and to study cell biology.

Dissertation Research - University of London - UK 1978 - 1981

As a graduate student at University College - University of London, conducted research under the supervision of Dr. F. L. Pierce, on the immunobiology and pharmacology of mast cells and basophils and their role in allergic disorder and asthma. Studied the processes that sensitized these cells and led to hypersensitivity reactions, signal transduction mechanisms and the role of calcium during their activation, degranulation and release of inflammatory mediators, pharmacological regulation by anti-allergic drugs, and the mechanism of action of these drugs. This research led to the publication of 12 papers including a publication in Nature, and to a Ph.D. degree in Biological Chemistry from the University of London in 1981.

EDUCATION

Ph.D., Biological Chemistry - 1978-1981
Department of Chemistry, University of London (University College), London, U.K.

B.Sc. (Hons) Biochemistry - 1973-1976
Dept. of Biochemistry, University of London (Queen Elizabeth/Bedford College), London, U.K.

ASSOCIATIONS & HONORS

Current and Past Membership

- Society for Leukocyte Biology (1999 - Present)
- Inflammation Research Association (1996 – Present)
- American Association of Immunologists (1986 - Present)
- Society for Analytical Cytology (1984 - 1997)
- American Association for the Advancement of Sciences (1986 - 1996)

- New York Academy of Sciences (1985 - 1996)
- British Biochemical Society (1979 - 1988)
- British Society for Immunology (1980 - 1987)
- British Society for Cell Biology (1980 - 1982)

Associtate Editor: Current Molecular Medicine

Fellowships, Honors and Awards

- INSERM, Visiting Scientist (1983)
- EMBO Fellow (1982-83)
- World University Service Scholar (1978-81, U.K.)
- British Council Scholarship (1973-76)
- Invited Faculty for NATO Advanced Courses in Flow Cytometry (Paris-1984, 1985, 1988, 1992, 1995; Hershey, PA-1985, Philadelphia, 1986)
- Invited speaker in a number of National and International Scientific Meetings
- Animal Welfare Award (given by R&D Chairman), SmithKline Beecham - 1996
- Impact Award, Clenoliximab (CD4 mAb) Project Team Leader, SmithKline Beecham - 1998
- Simply the Best Award (given by R&D Chairman), 7TM (GPCR) Strategic Initiative Team, SmithKline Beecham - 2000

PUBLICATIONS & PATENTS

Publications:

- 102 refereed articles and reviews
- Over 120 abstracts

Patents (issued or pending):

- 24 patents
- 17 issued, 7 applications pending

Publications

1. Kensil, C., Read, A.X. Mo, and A. Truneh, *Current vaccine adjuvants: An overview of a diverse class.* Frontiers in Bioscience, 2004. **9**: p. 2972-2988.

2. Morel, Y., Truneh, A., Costello, R. T., and Olive, D., *LIGHT, a new TNF superfamily member, is essential for memory T helper cell-mediated activation of dendritic cells.* Eur J Immunol, 2003. 33(11): 3213-9.

3. Federici, M. M., Venkat, K., Bam, N., Patel, K., Dal Monte, P. R., Fernie, B., Hensley, P., Carr, S., Baldoni, J., Truneh, A., and Erickson, J., *Detection and consequences of recombinant protein isoforms: implications for biological potency.* Dev Biol (Basel), 2003. 113: 53-7; discussion 113-4.

4. Costello, R. T., Mallet, F., Barbarat, B., Schiano De Colella, J. M., Sainty, D., Sweet, R. W., Truneh, A., and Olive, D., *Stimulation of non-Hodgkin's lymphoma via HVEM: an alternate and safe way to increase Fas-induced apoptosis and improve tumor immunogenicity.* Leukemia, 2003. 17(12): 2500-7.

5. Mason, U., Aldrich, J., Breedveld, F., Davis, C. B., Elliott, M., Jackson, M., Jorgensen, C., Keystone, E., Levy, R., Tesser, J., Totoritis, M., Truneh, A., Weisman, M., Wiesenhutter, C., Yocum, D., and Zhu, J., *CD4 coating, but not CD4 depletion, is a predictor of efficacy with primatized monoclonal anti-CD4 treatment of active rheumatoid arthritis.* J Rheumatol, 2002. 29(2): 220-9.

6. Davenport, C. M., McAdams, H. A., Kou, J., Mascioli, K., Eichman, C., Healy, L., Peterson, J., Murphy, S., Coppola, D., and Truneh, A., *Inhibition of pro-inflammatory cytokine generation by CTLA4-Ig in the skin and colon of mice adoptively transplanted with CD45RBhi CD4+ T cells correlates with suppression of psoriasis and colitis.* Int Immunopharmacol, 2002. 2(5): 653-72.

7. Newman, R., Hariharan, K., Reff, M., Anderson, D. R., Braslawsky, G., Santoro, D., Hanna, N., Bugelski, P. J., Brigham-Burke, M., Crysler, C., Gagnon, R. C., Dal Monte, P., Doyle, M. L., Hensley, P. C., Reddy, M. P., Sweet, R. W., and Truneh, A., *Modification of the Fc region of a primatized IgG antibody to human CD4 retains its ability to modulate CD4 receptors but does not deplete CD4(+) T cells in chimpanzees.* Clin Immunol, 2001. 98(2): 164-74.

8. Morel, Y., Truneh, A., Sweet, R. W., Olive, D., and Costello, R. T., *The TNF superfamily members LIGHT and CD154 (CD40 ligand) costimulate induction of dendritic cell maturation and elicit specific CTL activity.* J Immunol, 2001. 167(5): 2479-86.

9. Fishman-Lobell, J., Tsui, P., Reddy, M., DiPrinzio, R., Eichman, C., Sweet, R. W., and Truneh, A., *CD4 mAb induced apoptosis of peripheral T cells: multiparameter subpopulation analysis by flow cytometry using Attractors.* J Immunol Methods, 2001. 257(1-2): 71-82.

10. R. W. Sweet and A. Truneh. *CD4* (Invited Review). Encyclopedia of Molecular Medicine, John Wiley & Sons, Inc. (Editor), 2001.

11. Davenport, C.M., A. Truneh. *The Role of Cytokines in Inflammatory Bowel Disease and Prospects for Cytokine Directed Therapy*. Submitted.

12. Davenport, C.M., A. Truneh. *Interleukin-2 knockout mice as a model for inflammatory bowel disease and evaluation of potential therapeutic agents*. Submitted.

13. Deen, K.C., Griego, S.D., Silverman, C.S., Davis, C.B., Truneh, A, and Sweet, R.W. *Monobody: a Monovalent Antibody with Favorable Pharmacokinetics In Vivo*, Submitted.

14. M. Reddy, K. Melnick, C. Kinney , C. Eichman, R. DiPrinzio, R. Sweet, and A. Truneh. *Expression of TRAIL and its receptors on freshly isolated lymphoid, myeloid cells and cell lines and implication for function. Leucocyte Typing VII, In press.*

15. M. Reddy, K. Melnick, C. Eichman, R. DiPrinzio, and A. Truneh. *T cell panel antigens on activated and non-activated T lymphocytes and monocytes and effects of mAbs on MLR. Leucocyte Typing VII, In press.*

16. Doyle, M. L., Brigham-Burke, M., Blackburn, M. N., Brooks, I. S., Smith, T. M., Newman, R., Reff, M., Stafford, W. F., 3rd, Sweet, R. W., Truneh, A., Hensley, P., & O'Shannessy, D. J. (2000). *Measurement of protein interaction bioenergetics: application to structural variants of anti-sCD4 antibody.* Methods in Enzymology, 323: 207-30.

17. Morel, Y., Schiano De Colella, J. M., Harrop, J., Deen, K. C., Holmes, S. D., Wattam, T. A., Khandekar, S. S., Truneh, A., Sweet, R. W., Gastaut, J. A., Olive, D., & Costello, R. T. (2000). *Reciprocal expression of the TNF family receptor herpes virus entry mediator and its ligand LIGHT on activated T cells: LIGHT down- regulates its own receptor.* J Immunol, 165: 4397-404.

18. Truneh, A., Sharma, S., Silverman, C., Khandekar, S., Reddy, M. P., Deen, K. C., McLaughlin, M. M., Srinivasula, S. M., Livi, G. P., Marshall, L. A., Alnemri, E. S., Williams, W. V., and Doyle, M. L. *Temperature-sensitive differential affinity of TRAIL for its receptors. DR5 is the highest affinity receptor.* J Biol Chem 275, 23319-25 (2000).

19. P. J. Bugelski, D. J. Herzyk, S. Rehm, A. G. Harmsen, E. V. Gore, D. M. Williams, B. E. Maleeff, A. M. Badger, A. Truneh, S. R. O'Brien, R. A. Macia, P. J. Wier, D. G. Morgan and T. K. Hart. (2000) *Preclinical Development of Keliximab, a PRIMATIZED™ Anti-CD4 Monoclonal Antibody, in Human CD4 Transgenic Mice: Characterization of the Model and Safety Studies.* Human and Experimental Toxicology, 19(4): 230-243.

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following administration to murine and nonhuman primate muscle. Journal of Virology, 74: 2420-2425.

23. Chirmule, N., Truneh, A., Haecker, S. E., Tazelaar, J., Gao, G. P., Raper, S. E., Hughes, J. V., & Wilson, J. M. (1999). *Repeated administration of adenoviral vectors in lungs of human CD4 transgenic mice treated with a nondepleting CD4 antibody.* Journal of Immunology, 163: 448-455.

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26. Harrop, J., Spamanato, J., Reddy, M., Eichman, C., Diprinzio, R., Cook, R. M., Truneh, A. (1998). *Kinetics of expression of TNFR superfamily molecules & other cytokine receptors on activated CD4+ T cells.* Leukocyte Typing VI. (pp. 871-873), Garland Publishing Inc.

27. Tan, K. B., Harrop, J., Reddy, M., Young, P., Terrett, J., Emery, J., Moore, G., & Truneh, A. (1997). *Characterization of a novel TNF-like ligand and recently described TNF ligand and TNF receptor superfamily genes and their constitutive and inducible expression in hematopoietic and non-hematopoietic cells.* Gene, 20: 35-46.

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29. Sung, C. P., Arleth, A. J., Eichman, C., Truneh, A., & Ohlstein, E. H. (1997). *Carvedilol, a multiple-action neurohumoral antagonist, inhibits mitogen-activated protein kinase and cell cycle progression in vascular smooth muscle cells.* Journal of Pharmacology & Experimental Therapeutics, 283: 910-7.

30. Anderson, D., Chambers, K., Hanna, N., Leonard, J., Reff, M., Newman, R., Baldoni, J., Dunleavy, D., Reddy, M., Sweet, R., & Truneh, A. (1997). *A primatized MAb to human CD4 causes receptor modulation, without marked reduction in CD4+ T cells in chimpanzees: in vitro and in vivo characterization of a mAb (IDEC-CE9.1) to human CD4.* Clinical Immunology & Immunopathology, 84: 73-84.

31. Pages, F., Ragueneau, M., Klasen, S., Battifora, M., Couez, D., Sweet, R., Truneh, A., Ward, S. G., & Olive, D. (1996). *Two distinct intracytoplasmic regions of the T-cell adhesion molecule CD28 participate in phosphatidylinositol 3-kinase association.* Journal of Biological Chemistry, 271: 9403-9.

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33. Nunes, J. A., Battifora, M., Woodgett, J. R., Truneh, A., Olive, D., & Cantrell, D. A. (1996). *CD28 signal transduction pathways. A comparison of B7-1 and B7-2 regulation of the map kinases: ERK2 and Jun kinases.* Molecular Immunology, 33: 63-70.

34. Kariv, I., Truneh, A., & Sweet, R. W. (1996). *Analysis of the site of interaction of CD28 with its counter-receptors CD80 and CD86 and correlation with function.* Journal of Immunology, 157: 29-38.

35. Truneh, A., Reddy, M., Ryan, P., Lyn, S. D., Eichman, C., Couez, D., Hurle, M. R., Sekaly, R. P., Olive, D., & Sweet, R. (1996). *Differential recognition by CD28 of its cognate counter receptors CD80 (B7.1) and B70 (B7.2): analysis by site directed mutagenesis.* Molecular Immunology, 33: 321-34.

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37. Okafo, G. N., Burrow, L. M., Neville, W., Truneh, A., Smith, R. A. G., Reff, M., & Camilleri, P. (1996). *Simple Differentiation Between Core-Fucosylated and Nonfucosylated Glycans By Capillary Electrophoresis.* Analytical Biochemistry, 240: 68-74.

38. Hart, T. K., Truneh, A., & Bugelski, P. J. (1996). *Characterization of CD4-gp120 Activation Intermediates During Human Immunodeficiency Virus Type 1 Syncytium Formation.* AIDS Research & Human Retroviruses, 12: 1305-1313.

39. Truneh, A., Reddy, M., Ryan, P., Lyn, S., Kariv, I., Eichman, C., Couez, D., Hurle, M., Sekaly, R.-P., Olive, D. and Sweet, R. (1996) *Analysis of CD28 Interactions with its cognate counter-receptors CD80 and CD86.* In: A. Jacquemin-Sablon (Ed.) Flow and Imaging Cytometry (pp3-19), NATO ASI Series, Cell Biology, Vol. 95.

40. Patil Ashok, D., Kumar, N. V. A. S. A. N. T., Kokke Wilhelmus, C., Bean Mark, F., Freyer Alan, J., Brosse Charles, D. E., Mai, S. H. I. N. G., Truneh, A. L. E. M. S. E. G. E. D., Carte, B. R. A. D., & et al. (1995). *Novel Alkaloids from the Sponge Batzella Sp. Inhibitors of HIV-gp120-Human Cd4 Binding.* J. Org. Chem., 60: 1182-8.

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46. Pages, F., Ragueneau, M., Rottapel, R., Truneh, A., Nunes, J., Imbert, J., & Olive, D. (1994). *Binding of phosphatidylinositol-3-OH kinase to CD28 is required for T-cell signalling.* Nature, 369: 327-9.

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